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Original Article

Pattern of Coronary Artery Disease and Frequency of Left Circumflex Artery as a Culprit in Patients of Non-ST Elevation Acute Coronary Syndrome with a Normal Electrocardiogram

Sarwat Paiker Malik, Muhammad Nadir Khan, Sadaf Shabbir Kiani, Masood Khan, Fahad Khan Toru, Maida Anwar, Javeria Kamran*, Naseem Azad*

Department of Adult Cardiology, Armed Forces Institute of Cardiology/National Institute of Heart Diseases/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Department of R&D, Armed Forces Institute of Cardiology/National Institute of Heart Diseases/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To determine the pattern of Coronary Artery Disease in patients presenting with Non ST-Elevation Acute Coronary Syndrome(NSTE-ACS) with a normal Electrocardiogram (ECG) and to assess the frequency of left circumflex artery as a culprit artery.

Study Design: Analytical Cross-sectional Study.

Place and Duration of Study: In Armed Forces Institute of Cardiology/National Institute of Heart Diseases Rawalpindi, Pakistan, from Aug 2022 to Jan 2023.

Methodology: A total of n=118 patients with NSTE-ACS, presenting within 24-hours of symptoms onset, with a normal ECG reports, were recruited using non-probability consecutive sampling. Demographics, Ejection fraction, and Coronary angiography findings were noted. Coronary Angiography was done as per standard protocol. The number of diseased vessels was recorded. Data management and analysis were done on SPSS version-26;00. Mean±SD along with frequencies & percentages were used to express quantitative and qualitative variables respectively. Chi square and Student t-test were applied and *p*-value <0.05 was taken as statistically significant.

Results: Out of the 118 patients, 86(72.0%) were males. Mean age of the patients was 60.26±9.67 years. The coronary angiography showed Triple Vessel Coronary Artery Disease (TVCAD) in 50(42.4%) patients, double and single vessel coronary artery disease in 22(18.6%) and 43(36.4%) patients, respectively. The culprit artery was found to be Left circumflex artery in 77(65.3%), left anterior descending in 69(58.5%) and Right coronary artery in 49(39.0%) of the patients.

Conclusion: Majority of the patients with normal ECG and NSTE-ACS had TVCAD and the Left Circumflex artery was the most common Culprit in such patients.

Keywords: Coronary Artery Disease, Culprit Artery, Electrocardiogram, Left Circumflex Artery, Non-ST Elevation Acute Coronary Syndrome.

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INTRODUCTION

Chest pain is one of the foremost reasons to seek medical care.[1] Whenever, the blood supply of the heart is affected either due to rupture of atherosclerotic plaque or due to occlusion of one of the main vessels supplying the heart, it leads to a wide range of symptoms including severe central chest discomfort, diaphoresis, and/or pain radiating to jaw, shoulder, arm, neck, back, upper abdomen, collectively recognized under the umbrella term of Acute Coronary Syndrome (ACS). It encompasses two components 1) ST-elevation ACS (STE-ACS) and Non ST-Elevation ACS (NSTE-ACS) patients with flattened/inversion of T waves, persistent or transient ST-segment changes or no changes at all. NSTE-ACS is further categorized based on the troponin levels as either Non-ST Segment Elevation Myocardial Infarction (NSTEMI) with positive troponin levels or Unstable Angina (UA) with normal troponin levels.[2] CAD has become a global health issue in the recent era. Global Burden of Disease (GBD) estimated that 43% of all Cardiovascular deaths are related to CAD.[3,4] The American Heart Association estimated that more than 17.6 million deaths per year were caused by cardiovascular disease in 2016.[5] For prompt diagnosis of suspected ACS, the initial 12-lead ECG plays a significant role as a quick diagnostic tool in Emergency Department (ED) preferably conducted and analyzed within 10 minutes of presentation.[6] Studies showed that at the time of presentation in ED , low-risk patients presenting with chest pain can be identified by clinical evaluation and 12-lead ECG. Unfortunately, ECG only has a limited sensitivity of 50-60% for the diagnosis of ACS due to its restricted

Correspondence: Dr Sarwat Paiker Malik, Department of Adult Cardiology, Armed Forces Institute of Cardiology/NIHD, Rawalpindi Pakistan

ability to detect ischemia,[7] particularly in the LCX territory or in patients with previous AMI or in the true posterior left ventricular region.[8] Additionally, the presence of ischemia in ECG can also be transient.[9] The patients having normal ECG with chest pain are frequently neglected or are considered low risk. The study aimed to identify the patient population that may have aggressive or severe CAD despite having normal ECG and those who had an impending risk of MI, due to the nature of occlusion, i.e., subtotal or thrombotic. This study aimed to increase the body of knowledge on LCX involvement as culprit vessel, enabling earlier detection and reducing delayed revascula-rization. The present study adds useful information to the available contemporary data.

METHODOLOGY

This Analytical Cross-Sectional study was conducted Armed Forces Institute of Cardiology/ National Institute of Heart Diseases Rawalpindi, Pakistan from August 2022 to January 2023. Non-probability consecutive sampling was used to select the study participants. The study was conducted after approval from the Institutional Ethical Review Board (IERB letter #9/2/R&D/2022/204).

Sample size was estimated by taking a 17% prevalence of NSTEMI,[10] with a normal ECG in the general population, using the World Health Organization sample size calculator yielding a sample size of (n=39) with a 90% confidence interval and margin of error at 10%. However, data was collected from 118 study participants.

Inclusion Criteria: All patients including males and females, aged >18 years, with a confirmed diagnosis of NSTE-ACS having normal ECG underwent coronary angiography with co-morbidities like Diabetes Mellitus (DM), Hypertension (HTN), smoking, dyslipidemia were included.

Exclusion Criteria: Patients with ECG changes such as; pathological Q waves, any ST-T segment changes, ST-sagging, left Ventricular Hypertrophy, and axis deviation or bundle branch blocks were excluded. Patients with STE-ACS, undergoing fibrinolysis, cardiogenic shock, acute left Ventricular Failure and pregnant females were not enrolled in the study.

Patients' demographics, co-morbids, Troponin I and CK levels, Ejection fraction and data from Coronary Angiography reports were noted on data collection proforma. Coronary artery stenosis was documented as mild, moderate and critical after viewing Coronary angiogram. Pattern of coronaries involvement was noted as Triple Vessel (TVCAD), Double Vessel (DVCAD) and Single Vessel Coronary Artery Disease (SVCAD). NSTE-ACS was further categorized as: NSTEMI involving myocardial necrosis, without immediate ST-segment elevation, as shown by rise of serum cardiac markers; troponin I or troponin T and CK.[1] Unstable angina: Patients having ischemic chest pain at rest for more than 20 minutes, with or without ECG changes and normal cardiac biomarkers. This also included patients with new onset angina, angina of increasing frequency and duration.[1] The Culprit artery was defined as the artery which has recent total or subtotal occlusion with thrombus, or the artery having the most severe stenosis in the absence of above mentioned criteria.[11] Significant stenosis was considered if 50% or greater in the left main coronary artery, coronary artery stenosis of ≥70% or greater in any other coronary artery, or both.[12,13]

Statistical Package for Social Sciences (SPSS) version 26:00 was used for data management and analysis. Quantitative and qualitative variables were presented as mean & standard deviations and percentages & frequencies respectively. Qualitative variables were compared using the Chi-square test and mean difference was found by student-t test. $p \leq 0.05$ was taken significant.

RESULTS

Total (n=118) patients were enrolled over six months duration, meeting inclusion criteria and exclusion criteria as outlined above. Majority were males 86(72.9%) while 32(27.1%) were females .The average age of the patients was 60.26±9.67 years. The descriptive statistics and cross tabulation of comorbids with NSTE-ACS of study participants are presented in Table-I.

In our study, NSTE-ACS was associated significantly with smoking with p-value of <0.001.

It is significant to note that NSTE-ACS, as confirmed by a thorough evaluation of cardiac biomarkers, especially Troponin I and CK-MB was seen raised in 30 patients hence NSTEMI was diagnosed.

Angina symptoms were noted in 29(24.6%) patients atypical symptoms in 18(15.3%), and typical chest pain was noted in 68(57.6%) patients, while 2(1.7%) of patients had no symptoms initially as shown in Table-II. The pattern of coronaries with frequency of occluded vessels has been presented in Figure.

Table-I: Association of Comorbid Status with NSTE-ACS of the Study Sample (n=118)

Variables	Frequency(%) (n=118)	NSTE-ACS		*p*-value
		UA(n=88) Frequency(%)	NSTEMI(n=30) Frequency(%)	
Gender				
Males	86(72.9)	61(69.3)	25(83.3)	0.21
Females	32(27.1)	27(30.7)	5(15.6)	
Age(Years) Mean±SD	60.26±9.67	60.85±8.82	58.48±11.8	0.33
LVEF(%) Mean±SD	56.57±7.03	57.56±5.62	53.6±9.64	0.04
Diabetes Mellitus				
Yes	48(40.7)	37(42.0)	11(36.7)	0.76
No	70(59.3)	51(58.0)	19(63.3)	
Hypertension				
Yes	72(61)	52(59.1)	20(66.7)	0.60
No	46(39)	36(40.9)	10(33.3)	
Smoking				
Yes	24(20.3)	11(45.8)	13(54.2)	0.001
No	94(79.7)	77(81.9)	17(18.1)	
Dyslipidemia				
Yes	31(26.3)	21(23.9)	10(33.3)	0.43
No	87(73.7)	67(76.1)	20(66.7)	
Family history of IHD				
Yes	30(25.4)	26(29.5)	4(133.3)	0.12
No	88(74.6)	62 (70.5)	26(29.5)	
Troponin I				
Normal	88(74.6)	88(100.0)	-	<0.001
Raised	30(25.4)	-	30(100.0)	

**IHD= Ischemic Heart Disease, LVEF= Left Ventricular Ejection Fraction*

Table-II: Frequency of symptoms on presentation in Emergency Department (n=118)

Symptoms	NSTE-ACS		*p*-value
	UA (Total=88) Frequency (%)	NSTEMI (Total=30) Frequency(%)	
Angina	23(26.1)	6(20.0)	0.19
Atypical Chest Pain	16(18.2)	2(6.7)	
Borderline ETT	1(1.1)	0(0.0)	
No Symptoms	2(2.3)	0(0.0)	
Typical Chest Pain	46(52.3)	22(73.3)	

ETT=Exercise Test Tolerance; UA=Unstable Angina

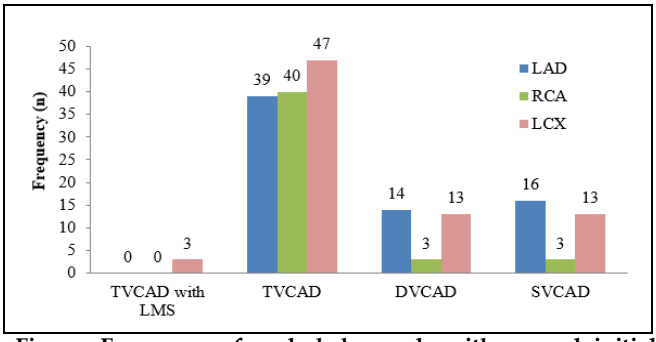

Figure: Frequency of occluded vessels with normal initial ECG (n=118)

TVCAD= Triple Vessel Coronary Artery Disease, DCVAD=Double Vessel Coronary Artery Disease, SVCAD= Single Vessel Coronary Artery Disease

The coronary angiography showed TVCAD in 50(42.4%) patients, Double and Single Vessel Coronary Artery Disease in 22(18.6%) and 43(36.4%) patients, respectively.

Table-III depicts LCX as the most common culprit as it was critically stenosed in 77(65.3%) patients of NSTE-ACS, with a normal ECG, followed by LAD 69(58.5%) and RCA 46(39%) respectively.

DISCUSSION

This study was aimed to determine the Pattern of CAD and frequency of the left circumflex artery disease in NSTE-ACS among patients with a normal ECG visiting AFIC.

ECG is a significant and first-line tool to evaluate patients presenting with chest pain in ED.[14] When presenting to the emergency room, quite a few patients with NSTE-ACS may have normal ECG readings, demonstrating that ECG may be an insufficient technique to diagnose ACS in many circumstances.[15] Turnip *et al.*[16] noticed 17% incidence of ACS in patients presenting with chest pain with a normal ECG. Chase *et al.*[17] found a 2.8% frequency of Acute MI in ED patients with an unremarkable ECG.

Table-III: Severity of Coronary Arteries Involvement (n=118)

NSTE-ACS	LAD					
	Critical (n=69) Frequency (%)	Mild (n=13) Frequency (%)	Moderate (n=17) Frequency (%)	Normal (n=19) Frequency (%)	Total (n=118)	*p*-value
UA	51(73.9)	11(84.6)	15(88.2)	11(57.8)	88	0.05
NSTEMI	18(26.1)	2(15.4)	2(11.8)	8(42.1)	30	
	RCA					
	Critical (n=46)	**Mild (n=2)**	**Moderate (n=12)**	**Normal (n=58)**	**Total (n=118)**	***p*-value**
UA	38(82.6)	2(100)	10(83.3)	38(65.5)	88	0.16
NSTEMI	8(17.4)	0(0)	2(16.7)	20(34.5)	30	
	LCX					
	Critical (n=77)	**Mild (n=1)**	**Moderate (n=6)**	**Normal (n=34)**	**Total (n=118)**	***p*-value**
UA	53(68.8)	1(100.0)	5(83.3)	29(85.3)	88	0.26
NSTEMI	24(31.2)	0(0)	1(16.7)	5(14.7)	30	

UA= Unstable Angina; NSTE-ACS = Non-ST Elevated Acute Coronary Syndrome; NSTEMI= Non ST-Elevated Myocardial Infarction

Normal ECG may not always be considered a benign result. This challenges the doctor to acquire a meticulous clinical and biochemical characterization on a practical level. A study conducted on NSTEMI with Normal ECG at Tabba Heart Institute, Karachi, Pakistan,[10] showed that out of 215 patients with ACS, having an unremarkable ECG within 24 hours of the onset of symptoms, 22.8%were confirmed as NSTEMI.

Welch *et al.*[18] reported that patients with chest pain who presented with a normal ECG had a mortality of 5.7% and a serious cardiac event in 19.2%.

Left circumflex artery as culprit is often missed by the standard 12-lead ECG.[19] Due to the lack of considerable ST-T changes on the 12- lead standard electrocardiograms; (LCX) blockage is frequently classified as NSTE-ACS.[20] Setianto *et al*. reported that around 30% of patients with total occlusion in LCx present with no significant ST-T changes or ST-segment elevation on ECG recording.[21] Khan *et al*.[22] found that Left Circumflex (LCx) accounted for 33% of patients with an initial NSTE-ACS diagnosis. The reason could possibly be due to smaller infarct size, incomplete occlusion of the vessel and smaller loss of total mass of myocardium in LCx related ACS. LCx usually supplies the posterior and lateral walls of the left ventricle, which are not well diagnosed by the 12 standard ECG leads ,resulting in a delay in diagnosis and early intervention such as Percutaneous Reperfusion/revisualization, often leading to worst outcome and greater infarct size.[23]

The pattern of involvement of coronaries in patients of NSTE-ACS with an unremarkable ECG was also found in our study. LCX was found as the most common culprit as it was critically stenosed in 65.3% patients of NSTE-ACS, with a normal ECG, followed by LAD and RCA respectively. Similar studies were conducted where Ahmad *et al.*[24] noticed that 68.3% of NSTEMI was due to occlusion of LAD artery followed by 49.6% due to RCA and 40.3% due to occlusion of LCX artery. Another study by Halim *et al.*[25] showed that among 1774 patients of high-risk NSTE-ACS who had culprit arteries other than LMS, a bypass graft, or a vascular branch ,the culprit was the LCX in 560(31.6%), RCA in 561(31.6%) and LAD in 653(36.8%).

LIMITATIONS OF STUDY

Firstly, the current study had smaller sample size and was a single-center study .Therefore the results obtained cannot readily be generalized. Secondly, only patients with main symptoms of "chest pain," and unstable angina were included while patients with stable angina equivalents were excluded. Our ACS definition included coronary artery stenosis of ≥70%; which may include patients with "stable" angina, rather than ACS. We also only looked at the initial ED ECG; while the serial ECG of patients with typical chest pain was not observed. More detailed prospective studies with larger sample size are needed in future to cover all aspects in more detail.

CONCLUSION

It was concluded that left Circumflex artery was the most common culprit vessel with 65.3% critical involvement, and majority of the patients presenting with NSTE-ACS with a normal ECG had TVCAD among patients presenting within 24-hours of symptoms onset on a background of unremarkable ECG findings. Unremarkable ECG findings should be evaluated meticulously as well as categorically complemented with the evaluation of cardiac enzymes to conclusively ascertain the absence of an NSTE-ACS.

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Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript:

SPM, MNK & SSK: Manuscript Writing, Data Analysis, Approval of the Final Version to be Published.

MK, FKT & MA: Data Acquisition, Critical Review, Approval of the Final Version to be Published.

JK & NA: Critical Review, Formatting, Drafting the Manuscript, Approval of the Final Version to be Published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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